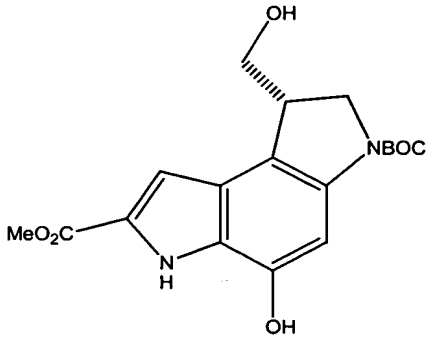
Remarks

Claims 1-9 and 31 are pending after entry of the foregoing amendments. Claims 10-30 have been cancelled without prejudice to presentation in a divisional application because they are drawn to non-elected subject matter. Claim 31 is allowed.

Claims 1-9 stand rejected under 35 U.S.C. §102(a) as unpatentable over Boger et al. Boger et al. teaches a total synthesis of (+)-duocarmycin SA, a naturally occurring and exceptionally potent antitumor antibiotic. Compounds 14, 15, and 18 of Boger et al. are as follows:



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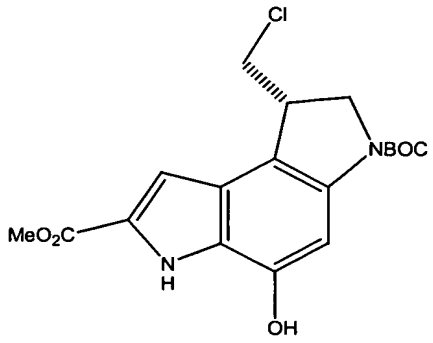

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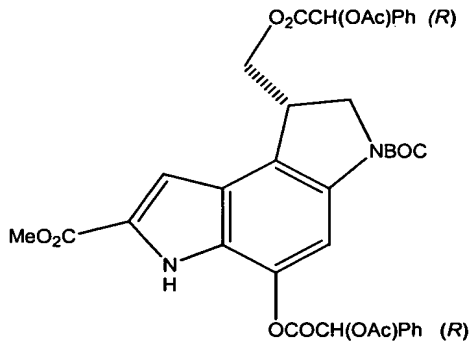

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Compound 18 is the bis-(*R*)-O-acetylmandelate ester of compound 14, which is used to resolve compound 14. (Declaration of Dr. Philip Howard ("Howard Decl.") at ¶s 6 and 7.)

Applicants respectfully submit that compounds 14 and 15 of Boger et al. do not anticipate claim 1 of the present application. When the A-B ring of formula **I** is pyrrole, Y is -O-Prot. "Prot" is defined as a protecting group at page 3, lines 19-20 of the specification. The term "protecting group" is further defined as having the usual

meaning in synthetic chemistry, i.e. any group which may be covalently bound to the protected atom and permits reactions to be carried out on the molecule having the protecting group without its removal, but is able to be removed without affecting the remainder of the molecule. (Page 5, line 23 – page 6, line 1.) Compounds 14 and 15 of Boger et al. have an unprotected hydroxyl at the 6-position. (Howard Decl. at ¶ 8.) Thus, compounds 14 and 15 of Boger et al. do not anticipate claim 1.

It is also Applicants' position that compound 18 of Boger et al. does not anticipate claim 1. In the claimed invention, X is an electrophilic leaving group. The term "electrophilic leaving group" is defined as a group that is readily eliminated from the molecule and carries with it an electron pair. (Page 7, lines 9-10.) The O-acetylmandelate ester of compound 18 is not an electrophilic leaving group and would not be used as such by one of ordinary skill in the art. (Howard Decl. at ¶ 9.) Thus, claim 1 is not anticipated by compound 18 of Boger et al.

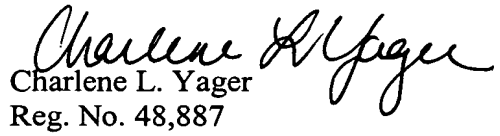
Applicants respectfully submit that claims 2-9 are not anticipated by Boger et al. for at least the reasons discussed with respect to claim 1.

Thus, Applicants respectfully submit that the claimed invention is not taught or suggested by the disclosure of Boger et al. and request that the rejection of claims 1-9 under §102(b) be withdrawn.

Applicants also respectfully request clarification that the previous rejection over Denny et al. was withdrawn.

In view of the foregoing, Applicants submit that the claims are in condition for allowance. Should the Examiner have any unanswered questions, please contact the undersigned at the phone number below.

Respectfully submitted,



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CIPE JC42 JUL 14 2004 PATENT & TRADEMARK OFFICE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
Group Art Unit 1624

I, Julie Mallder, hereby certify that this correspondence is being deposited with the US Postal Service in an envelope as "Express Mail Post Office to Addressee," Mailing Label No. EV 086435506 US addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on ~~June~~ July 14, 2004.

Julie Mallder
Signature

July 14, 2004
Date of Signature

In re

Patent Application of

David Edwin Thurston, et. al.

Application No. 10/069,202

Confirmation No. 1583

Filed: February 22, 2002

Examiner: Bruck Kifle

"CYCLOPROPYLINDOLE DERIVATIVES"

DECLARATION UNDER 37 C.F.R. 1.132

I, Dr. Philip Howard, declare as follows:

1. I have personal knowledge of the following facts and I make this declaration in support of the prosecution of U.S. Patent Application Serial No. 10/069,202 before the United States Patent and Trademark Office.

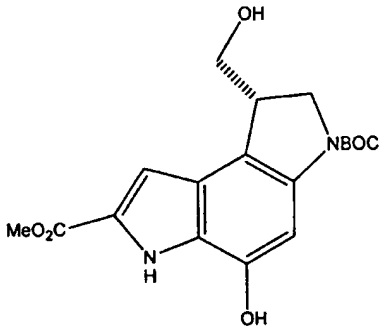
2. I am currently employed Vice-President (Chemistry) at SpiroGen Limited, a position I have held since June 2003 (full time). Prior to that I was employed as Senior Research Officer, University of London, School of Pharmacy.

3. My curriculum vitae is attached as Appendix A.

4. I am a co-inventor of the subject matter of the above-identified application and I am familiar with the art and with the prosecution history of this application.

5. I have reviewed the pending Office action and the cited reference. In particular, the Examiner asserts that Boger et al., *J. Am. Chem. Soc.* (1992), 114(25), 10056-58, teaches compounds that fall within the scope of the claimed invention.

6. Boger et al. teaches a total synthesis of (+)-duocarmycin SA, a naturally occurring and exceptionally potent antitumor antibiotic. Compounds 14, 15, and 18, which are cited by the Examiner as relevant to the pending claims, are as follows:



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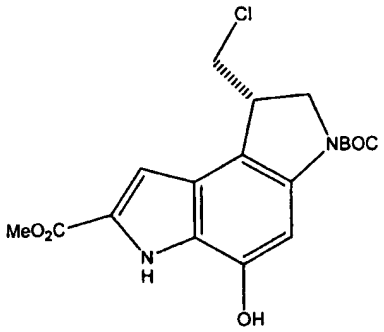

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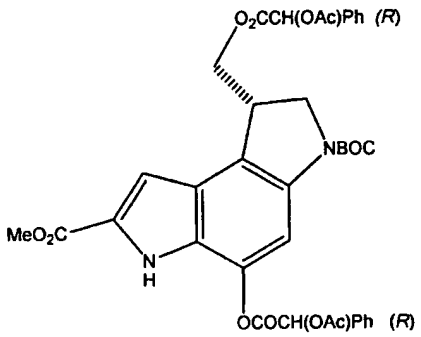

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7. Compound 18 is the bis-(*R*)-O-acetylmandelate ester of compound 14, which is used to resolve compound 14.

8. In claim 1 of the '202 application, Y is -O-Prot when the A-B ring is pyrrole. "Prot" is defined as a protecting group at page 3, lines 19-20 of the specification. The term "protecting group" is further defined as having the usual meaning in synthetic chemistry, i.e. any group which may be covalently bound to the protected atom and permits reactions to be carried out on the molecule having the protecting group without its removal, but is able to be removed without affecting the remainder of the molecule. (Page 5, line 23 – page 6, line 1.) Compounds 14 and 15 of Boger et al. do not have a protected hydroxyl at the 6-position.

9. In claim 1 of the '202 application, X is an electrophilic leaving group. The term "electrophilic leaving group" is defined as a group that is readily eliminated from the molecule and carries with it an electron pair. (Page 7, lines 9-10.) The O-acetylmandelate ester of compound 18 is not an electrophilic leaving group and would not be used as such by one of ordinary skill in the art.

10. I hereby declare that all statements made herein of my own knowledge are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated this 5 day of July, 2004.

Dr. Philip Howard